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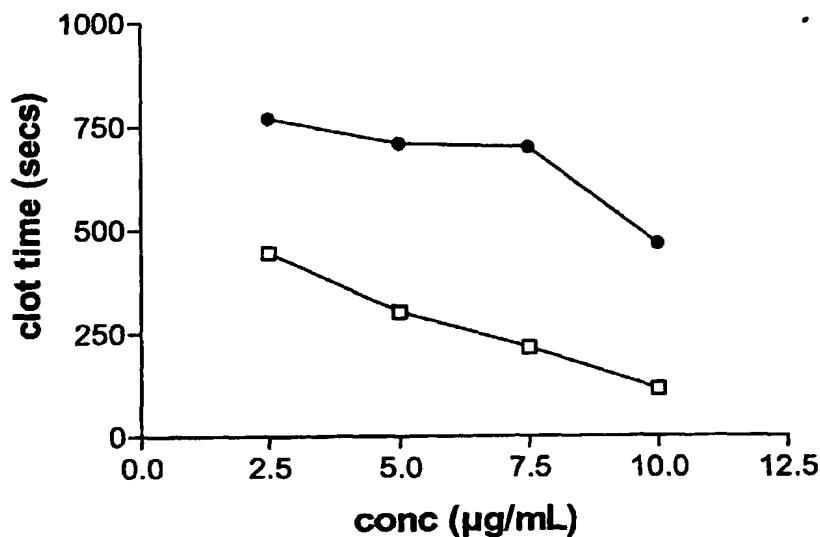
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60/479,708 19 June 2003 (19.06.2003) US
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- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,

[Continued on next page]

(54) Title: FVII OR FVIIa VARIANTS



(57) Abstract: Variants of FVII or FVIIa comprising at least one amino acid modification in position 196, 237 or 341 relative to hFVII or hFVIIa. The variants exhibit an increased clotting activity, i.e. reduced clotting time, compared to rhFVIIa.

● rhFVIIa
□ G237GAA



TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

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4 November 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

Internat. Application No
PCT/UK2004/000193

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N9/64 C12N15/57 A61K38/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBL, WPI Data, PAJ, EMBASE, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/58935 A (MAXYGEN APS) 16 August 2001 (2001-08-16) cited in the application abstract; claims 1-73 page 29, line 20 - page 30, line 14	1-5, 28-35, 41,54-68
Y		36-40, 42-49,53
A	----- -/--	6-16

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

6 July 2004

Date of mailing of the international search report

28 SEP 2004

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Wiame, I

INTERNATIONAL SEARCH REPORT

Interr Application No
PCT/DK2004/000193

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ZHANG E ST ET AL: "Structure of extracellular tissue factor complexed with factor VIIa inhibited with a BPTI mutant" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 285, no. 5, 5 February 1999 (1999-02-05), pages 2089-2104, XP004464317 ISSN: 0022-2836 abstract; figures 1,4; table 2 page 2093, column 2, last paragraph - page 2095, column 1, paragraph 1 -----	5,17-27
Y	SHAH A ET AL: "Manipulation of the membrane binding site of vitamin K-dependent proteins: enhanced biological function of human factor VII" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 95, no. 8, 14 April 1998 (1998-04-14), pages 4229-4234, XP002092845 ISSN: 0027-8424 abstract page 4232, column 2; figure 4 page 4229 -----	5,17-27, 36-40, 42-53
Y	WO 02/22776 A (NOVO NORDISK AS ; PERSSON EGON (DK); OLSEN OLE HVILSTED (DK)) 21 March 2002 (2002-03-21) page 46 -----	50-52
X	DATABASE EMBL 2 February 2003 (2003-02-02), "Gallus gallus anticoagulant protein C precursor (PROC) mRNA, complete cds" XP002286589 Database accession no. AF465270 the whole document -----	1-4,6-8, 14,15, 17-22, 27-37, 42,47, 50-55,59
X	DATABASE UNIPROT 1 August 1991 (1991-08-01), "Coagulation factor VII (EC 3.4.21.21) (Serum prothrombin conversion accelerator)" XP002286590 Database accession no. P22457 the whole document -----	1-4, 17-21, 27-36, 38-41, 50,54, 55,59
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INTERNATIONAL SEARCH REPORT

Intern - Application No
PCT/DK2004/000193

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>IAKHIAEV A ET AL: "THE ROLE OF CATALYTIC CLEFT AND EXOSITE RESIDUES OF FACTOR VIIA FOR COMPLEX FORMATION WITH TISSUE FACTOR PATHWAY INHIBITOR" THROMBOSIS AND HAEMOSTASIS, STUTTGART, DE, vol. 85, 2001, pages 458-463, XP002909201 ISSN: 0340-6245 page 4229</p> <p>-----</p>	
A	<p>CHANG Y-J ET AL: "ENGINEERED RECOMBINANT FACTOR VII Q217 VARIANTS WITH ALTERED INHIBITOR SPECIFICITIES" BIOCHEMISTRY, AMERICAN CHEMICAL SOCIETY. EASTON, PA, US, vol. 38, no. 34, 1999, pages 10940-10948, XP002908092 ISSN: 0006-2960 abstract</p> <p>-----</p>	

INTERNATIONAL SEARCH REPORT

In tional application No.
PCT/DK2004/000193

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☒ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK2004/000193

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 65 to 68 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-68 all partially and in as far as applicable

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 65 to 68 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.1

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-68 (all partially and in as far as applicable)
human factor VII(a) variants comprising at least a mutation
in position 196 and uses thereof

2. claims: 1-68 (all partially and in as far as applicable)
human factor VII(a) variants comprising a at least a
mutation in position 237 and uses thereof

3. claims: 1-68 (all partially and in as far as applicable)
human factor VII(a) variants comprising a at least a
mutation in position 341 and uses thereof

INTERNATIONAL SEARCH REPORT

nation on patent family members

Intern^o Application No

PCT/DK2004/000193

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